

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



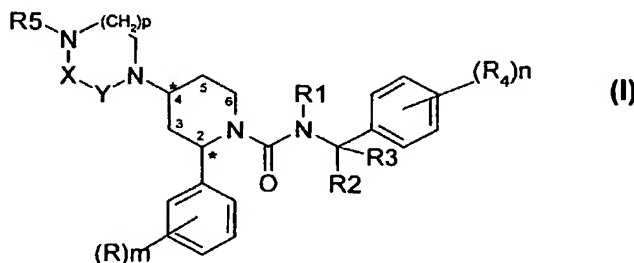
(43) International Publication Date
14 August 2003 (14.08.2003)

PCT

(10) International Publication Number
WO 03/066621 A1

- (51) International Patent Classification⁷: C07D 401/04, A61K 31/496, A61P 25/00 (74) Agent: THOMSON, Clive, Beresford; CN925.1, 980 Great West Road, Brentford, Middlesex TW7 9GS (GB).
- (21) International Application Number: PCT/GB03/00501 (81) Designated States (*national*): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (22) International Filing Date: 5 February 2003 (05.02.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data: 0203022.9 8 February 2002 (08.02.2002) GB (84) Designated States (*regional*): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).
- (71) Applicant (*for all designated States except US*): GLAXO GROUP LIMITED [GB/GB]; Glaxo Wellcome House, Berkeley Avenue, Greenford, Middlesex UB6 0NN (GB).
- (72) Inventors; and (75) Inventors/Applicants (*for US only*): ALVARO, Giuseppe [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming 2, I-37135 Verona (IT). DI FABIO, Romano [IT/IT]; GlaxoSmithKline SpA, Via Alessandro Fleming, 2, I-37135 Verona (IT).
- Published:
— with international search report
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*

(54) Title: PIPERIDINE DERIVATIVES AND THEIR USE AS ANTAGONISTS OF TACHYKININS



(57) Abstract: The present invention relates to piperidine derivatives of formula (1) Wherein R represents halogen or C₁₋₄ alkyl; R₁ represents hydrogen or C₁₋₄ alkyl; R₂ represents hydrogen, C₁₋₄ alkyl; R₃ represents hydrogen, C₁₋₄ alkyl; R₄ represents trifluoromethyl, C₁₋₄ alkyl, C₁₋₄ alkoxy, trifluoromethoxy or halogen; R₅ represents hydrogen, C₁₋₄ alkyl, C₃₋₇ cycloalkyl, C(O)R₆ or S(O)₂R₆; R₆ represents C₁₋₄ alkyl or C₃₋₇ cycloalkyl; m is zero or an integer from 1 to 3; n is an integer from 1 to 3; p is an integer from 1 to 2; X and Y are independently C(O) or CH₂; provided that i) X and Y are not both C(O) and ii) when X and Y are both CH₂ and p is 1, R₅ is not hydrogen, C₁₋₄ alkyl or C(O)R₆; and pharmaceutically acceptable salts and solvates thereof, the process for their preparation and their use in the treatment of condition mediated by tachykinins.

INTERNATIONAL SEARCH REPORT

Inter. Search Application No
PCT/GB 03/00501

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07D401/04 A61K31/496 A61P25/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07D A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, CHEM ABS Data, EMBASE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 16440 A (JANSSEN PHARMACEUTICA NV ;JANSSENS FRANS EDUARD (BE); SOMMEN FRANC) 9 May 1997 (1997-05-09) page 1, line 1 -page 4, line 15 ----	1-18
A	WO 01 25219 A (GLAXO GROUP LTD ;GIOVANNINI RICCARDO (IT); ST DENIS YVES (IT); ALV) 12 April 2001 (2001-04-12) page 1, line 1 -page 2, line 32 ----	1-18
P,X	WO 02 32867 A (GLAXO GROUP LTD ;TRANQUILLINI MARIA ELVIRA (IT); MARAGNI PAOLO (IT) 25 April 2002 (2002-04-25) page 1, line 1 -page 3, line 4; examples 1-19 -----	1-18

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

1 April 2003

Date of mailing of the international search report

08/04/2003

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Usuelli, A

INTERNATIONAL SEARCH REPORT

International Application No.
PCY/GB 03/00501

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claim 17 is directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compounds.
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Inter. Patent Application No

PCT/GB 03/00501

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9716440	A	09-05-1997	AT 188691 T	15-01-2000
			AU 704155 B2	15-04-1999
			AU 7493296 A	22-05-1997
			BR 9611184 A	30-03-1999
			CA 2234096 A1	09-05-1997
			CZ 9801322 A3	16-09-1998
			DE 69606196 D1	17-02-2000
			DE 69606196 T2	21-09-2000
			EA 980404 A1	29-10-1998
			WO 9716440 A1	09-05-1997
			EP 0862566 A1	09-09-1998
			ES 2143238 T3	01-05-2000
			GR 3033154 T3	31-08-2000
			HR 960507 A1	28-02-1998
			HU 9802985 A2	28-10-1999
			IL 123962 A	11-01-2001
			JP 11514634 T	14-12-1999
			JP 3073238 B2	07-08-2000
			NO 981534 A	24-06-1998
			NZ 321575 A	28-05-1999
			PL 327406 A1	07-12-1998
			PT 862566 T	30-06-2000
			SI 862566 T1	30-04-2000
			TR 9800756 T2	21-07-1998
			TW 460473 B	21-10-2001
			US 6197772 B1	06-03-2001
			US 6521621 B1	18-02-2003
			US RE37886 E1	15-10-2002
			ZA 9609090 A	29-04-1998
WO 0125219	A	12-04-2001	AU 7913900 A	10-05-2001
			BR 0014541 A	17-09-2002
			CN 1391564 T	15-01-2003
			CZ 20021166 A3	13-11-2002
			WO 0125219 A2	12-04-2001
			EP 1218359 A2	03-07-2002
			NO 20021637 A	06-06-2002
			TR 200200936 T2	22-07-2002
			US 2003028021 A1	06-02-2003
WO 0232867	A	25-04-2002	AU 9572301 A	29-04-2002
			WO 0232867 A1	25-04-2002